Individual Safety Report

3178308-X-00-01

For use by user-facilities, distributors and manufacturers for MANDATORY reporting

Approved by FDA on 10/29/93

Mfr report # 971222-107013552

UF/Dist report #:

FDA Use Only

JTB

A. Patient information

1. Patient Identifier: UNKNOWN — In confidence

2. Age at time of event: 30 Year(s) or Date of birth: [redacted]

3. Sex: [X] female [ ] male

4. Weight: ____ lbs or UNK ____ kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [ ] death ____ (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event: 02/19/92 (mo/day/yr)

4. Date of this report: 01/05/99 (mo/day/yr)

5. Describe event or problem

Notification via litigation of case summaries provided by physician/co-author of literature report (N Engl J Med 1997; 337:1112-7). Information provided based on extracted data from medical records of patients hospitalized for acetaminophen ingestion between 01-JAN-92 and 30-APR-95. According to extracted data, patient with history of cocaine use prior to admission unintentionally took Tylenol and TYLENOL WITH CODEINE #3 (30 tablets over 1.5 days prior to admission) for sore throat and pain in left knee. On 19-FEB-92, patient was admitted to ICU with portal systemic encephalopathy, adult respiratory distress syndrome, coagulopathy and acute liver failure. Admitting diagnoses was Tylenol overdose, sepsis, acute renal failure and dyspnea. On admission, patient was treated with N-acetylcysteine. Liver and renal consult noted. During hospital course patient developed oliguria and fibrosis. Fibrosis was treated with 18 chest tubes. Patient discharged on 25-JUN-92.

Note: This is a duplicate report of a case from McNeil Consumer Products Company reference #0904261A.

Follow-up information received 16-DEC-98: Medical records indicate the patient was seen in the emergency room on 17-FEB-92 and 18-FEB-92 for knee injury and discharged on TYLENOL With Codeine #3. On 19-FEB-92 the patient was seen in the emergency room (ER) at 0430 hours, diagnosed with

(Cont.)

6. Relevant tests/laboratory data, including dates

19-FEB-92 Creat 4.7, AST 32100, ALT 12700, AP 188, bili 4.1, GGT 119, PT 32.9, NH3 135, acetaminophen level 28, ETOH level was negative; 21-FEB-92 AST 4250, bili 9.1, PT 20.7; 27-FEB-92 Creat 1.1, AGT 64, AP 312, bili 23.5, Alb 2.1, PT 16.8; 26-APR-92 Creat 0.6, AST 37, AP 146, bili 0.7, PT 12.2

Follow-up information received 16-DEC-98: 19-FEB-98 temperature 36, pulse 125, blood pressure 84/palpable, respiration rate 30, pH 7.07, PCO2 37, PO2 60, O2 Sat 80%, NA 138, K 5.3, Cl 91, urea 29, creatinine 4.7, glucose 111, WBC

(Cont.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

No history of previous liver disease; ETOH history unclear but apparently no; prior to admission positive for cocaine

Follow-up information received 16-DEC-98: IV drug abuse and crack cocaine prior to admission, motor vehicle accident with knee surgery APR-91, no known drug allergies

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 TYLENOL WITH CODEINE #3 TABLETS (ACETAMINOPHEN & CODEINE)
#2 TYLENOL (ACETAMINOPHEN)

2. Dose, frequency & route used
#1 30 TAB/36 HOURS, ORAL
#2 Unknown, Unknown, ORAL

3. Therapy dates (if unknown, give duration) (from/to (or best estimate))
#1 02/18/92 - 02/19/92
#2 02/18/92 - 02/19/92

4. Diagnosis for use (indication)
#1 Sore throat, knee pain
#2 Sore throat, knee pain

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [ ] UNK [X] doesn't apply
#2 [ ] yes [ ] no [ ] UNK [X] doesn't apply

6. Lot # (if known)
#1 UNK
#2 UNK

7. Exp. date (if known)
#1 UNK
#2 UNK

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [ ] UNK [X] doesn't apply
#2 [ ] yes [ ] no [ ] UNK [X] doesn't apply

9. NDC # - for product problems only (if known)
NA

10. Concomitant medical products and therapy dates (exclude treatment of event)
1) UNKNOWN ??/??/?? - ??/??/??

G. All manufacturers

1. Contact office - name/address (& mfring site for devices)
R. W. JOHNSON PHARM. RESEARCH INSTITUTE
DIV. OF ORTHO PHARMACEUTICAL CORPORATION
ROUTE 202, P.O. BOX 300
RARITAN NJ 08869-0602

(Informing unit)

2. Phone number: (908) 704-4600

3. Report source (check all that apply)
- [ ] foreign
- [ ] study
- [X] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 12/16/98

5. (A) NDA # 85-055
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day [X] 15-day
- [ ] 10-day [ ] periodic
- [ ] Initial [X] follow-up # 1

8. Adverse event term(s)
1) ENCEPHALOPATHY
2) DYSPNOEA
3) COAGULATION DISORDER
4) HEPATIC FAILURE
5) SEPSIS
6) RENAL FAILURE ACUTE
7) PULMONARY FIBROSIS

(Cont.)

9. Mfr. report number: 971222-107013552

E. Initial reporter

1. Name, address & phone #
[redacted] MD
[redacted] MEDICAL CTR
[redacted]
Phone # [redacted]

2. Health professional? [X] yes [ ] no

3. Occupation: Physician

4. Initial reporter also sent report to FDA: [ ] yes [ ] no [X] unk

Form 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

JAN 07 1999

JAN 08 1999

Continuation Sheet for FDA-3500A Form

Mfr. report # : 971222-107013552

B.5 Describe event or problem (Cont...)

streptococcal pharyngitis and sent home. In the ER at 1325 hours that same day, the patient complained of epigastric pain and pleuritic chest pain. ER records list the patient ingested 30 tablets of TYLENOL with Codeine #3 over 1.5 days, but records include other acetaminophen dosing history, 50-60 tablets within 48 hours. The patient was diagnosed with hypotension and rule out sepsis and admitted. Subsequently the patient developed hepatic failure, hepatorenal syndrome and oliguria, respiratory distress, pulmonary fibrosis, multiple febrile spikes and an episode of hypertension secondary to sepsis. The patient was discharged home 09-JUN-92 on phenytoin, amitriptyline, aluminium carbonate, oxycodone with acetaminophen and pheniramine maleate. Principle diagnosis was acetaminophen overdose.

B.6 Relevant tests/laboratory data, including dates (Cont...)

32.5, HGB 14.3, HCT 43.1, platelets 385, phos 12.4, acetaminophen 28, salicylate 10, prothrombin time 32.8, partial prothrombin time 37.8, drug screen positive for cocaine and opiates, alcohol negative, AST 32100, ALT 12700, alkaline phosphatase 226, total bilirubin 4.1, CA 7.4

G. All manufacturers (Cont...)

G.8 Adverse event term(s)

8)PHARYNGITIS
9)CHEST PAIN
10)HYPOTENSION
11)THERAPEUTIC RESPONSE INCREASED
12)ABDOMINAL PAIN

Source of report (Literature)

Title	: ACETAMINOPHEN TOXICITY IN AN URBAN COUNTY HOSPITAL
Author	: FRANK SCHIODT, MD
Year	: 1997
Edition	: OCT 16
Journal Title	: NEW ENGLAND JOURNAL OF MEDICINE
Page No.	: 1112 To 1117